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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1817	4

DATE MAILED: 10/15/97

This is a communication from the examiner in charge of your application.

COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), No days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-6 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-6 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings which are acceptable for examination purposes until such time as allowable subject matter is indicated.

8. ☐ Allowable subject matter having been indicated, formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. These drawings are ☐ acceptable; ☐ not acceptable (see explanation).

10. ☐ The ☐ proposed drawing correction and/or the ☐ proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved. ☐ disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections MUST be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.

12. ☐ Acknowledgment is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

PTOL-326 (Rev. 7-82) EXAMINER'S ACTION

DRAWINGS

The drawings are objected to for reasons on the accompanying NOTICE OF DRAFTSPERSON'S PATENT DRAWING REVIEW (PTO-948). Correction is required.

The Figure and all references to the Figure in the specification should be amended to refer to --Figure 1--.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. **Correction of Informalities** -- 37 CFR 1.85; 1097 O.G. 36

New formal drawings must be filed with the changes incorporated therein. The art unit number, application number (including series code) and number of drawing sheets should be written on the reverse side of the drawings. Applicant may delay filing of the new drawings until receipt of the "Notice of Allowability" (PTO-37). If delayed, the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for response in the "Notice of Allowability" (PTO-37) to avoid extension of time fees. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a) for filing the corrected drawings (but not for payment of the issue fee). The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the three month shortened statutory period set in the "Notice of Allowability" (PTO-37). Within that three month period, two weeks should be allowed for review of the new drawings by the Office. If a correction is determined to be unacceptable by the Office, applicant must arrange to have an acceptable

correction re-submitted within the original three month period to avoid the necessity of obtaining an extension of time with extension fees. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

ABSTRACT REQUIRED

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

INFORMALITIES

The disclosure is objected to because of the following informalities: the "BACKGROUND OF THE INVENTION" and the "SUMMARY OF THE INVENTION" should be labelled separately.

Appropriate correction is required.

NON-ART BASED REJECTIONS

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 fail to recite clear, distinct and positive method steps; and, contain antecedent basis problems.

Claim 1 is inconsistent in reciting *plural* microorganisms in line 1 but *singular* microorganism in lines 3, 8 and 9 as well as *multiple* antibodies in line 3 forming a *singular* complex in line 4. It is unclear whether the intent is to detect multiple numbers of the same microorganism (e.g. 6-10 *Pseudomonas*) or to detect multiple different microorganisms (e.g. at least one microorganism selected from a predefined group such as *Pseudomonas, Bacillus, Serratia,* etc.) in the same sample. Claim 1 implies, rather than positively states, the "microorganism" being detected is a preselected microorganism. In the alternative, claim 1 is vague and indefinite in reciting multiple, undefined antibodies which generically specifically bind to any and all microorganisms. It is suggested that claim 1 be amended to state clearly the relationship between the antibody(ies), the microorganism(s), the antigen and the complex as well

as the relationship between the incident light energy, the lower resonance enhanced Raman backscattered energy and the characteristic spectral peak. Finally, claim 1 is vague and indefinite in reciting detection "based on" a characteristic spectral peak. It is unclear whether claim 1 requires the incident light to excite specific characteristic markers and the resonance enhanced Raman backscattered energy must then be converted into a spectrum which corresponds to these characteristic markers of the preselected microorganisms, followed by comparison to a reference resonance Raman spectrum; etc. Critical elements should be positively stated, not merely implied.

The claims are confusing in using inconsistent terminology. Specifically, the difference in scope between "comprising" and "containing" is unclear. If there is no difference, a single term should be used. If there is a difference, that difference should be clearly defined. See also "an antigen to antibody complex" (claim 1) and "the antigen antibody complex" (claim 5).

It is suggested that the superfluous "wherein the medium is a liquid medium" be deleted from claim 5, lines 1-2 as needlessly confusing in view of claim 2. Secondly, the relationship between the "detecting" steps of claims 5 and 1 is unclear, e.g. does claim 5 intend an additional detection step based upon other than the "characteristic spectral peak" of claim 1. If it is the same detecting step, then it is suggested that claim 5 be amended to recite simply a further step of removing the complex from the liquid medium prior to the contacting step of claim 1, or equivalent. Claim 5 is also confusing in returning to the term "microorganism" in line 6 because claims 3 and 4 have both been previously narrowed to a "bacterium".

It is unclear whether claim 6 is drawn to a device, i.e. a "system" as recited in its preamble, or to a method in view of the positively recited method step in its preamble. It is unclear what structural elements are actually present in the device; or, what method steps are actually occurring.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 1-6 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the specification as originally filed on page 4 which states

> A sample to be tested is placed in a medium, the medium containing *antibodies attached to a surface* for binding to a *specific microorganism* to form an antigen to antibody complex. (emphasis added)

and page 6 which states

> Sensitive detection is possible because of a prominent peak at 1485 cm^{-1} associated with nucleic acids of bacteria can be *selectively* and sensitively detected *in the presence of proportionately very much larger numbers of antibody* **if** *irradiation is with laser light in the range 242-257.*
>
> Previous UV spectral studies of bacteria and protein support that, if the bacteria-antibody complex can be detected using 242 nm light, that the approach will work for various wavelengths in the vicinity of 242-257 nm for which there is *little protein fluorescence interference* in the Raman fingerprint region, and specifically at 1485 cm^{-1}. (emphasis added)

and page 7 which states

> ...the invention...is equally applicable to the detection of any microorganism or other cells that contain nucleic acids (DNA and/or RNA).

None of claims 1-6 recite detection of a preselected microorganism using a solid phase antibody which specifically binds to a preselected antigen on the surface of the microorganism thereby immobilizing the microorganism on the solid phase where the antibody-antigen/microorganism complex is irradiated with laser light in the range of 242 to 257 nm in order to produce resonance enhanced Raman spectrum of backscattered lower energy based upon the DNA and/or RNA of the microorganism which is compared to a resonance enhanced Raman spectrum of backscattered lower energy known to be produced by the DNA and/or RNA of the preselected microorganism in the absence of background fluorescence interference.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method and system for detection of a preselected microorganism using a solid phase antibody which specifically binds to a preselected antigen on the surface of the microorganism thereby immobilizing the microorganism on the solid phase where the antibody-antigen/microorganism complex is irradiated with laser light in the range of 242 to 257 nm in order to produce resonance enhanced Raman spectrum of backscattered lower energy based upon the DNA and/or RNA of the microorganism which is compared to a resonance enhanced Raman spectrum of backscattered lower energy known to be produced by the DNA and/or RNA of the preselected microorganism in the absence of background fluorescence interference, does not reasonably provide enablement for generic detection of any microorganism, any wavelength of incident light, based on any backscattered energy and characteristic spectral peak of any characteristic marker or any generic antibody. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification specifically requires use of solid phase antibody which specifically binds to the microorganism to be tested for, optionally followed by a wash step, to isolate the microorganism to be tested for. As acknowledged in the specification on page 6,

> Sensitive detection is possible because of a prominent peak at 1485 cm^{-1} associated with nucleic acids of bacteria can be *selectively* and sensitively detected *in the presence of proportionately very much larger numbers of antibody* **if** *irradiation is with laser light in the range 242-257.*

No other identifying "fingerprint" marker for detection which is free of significant background fluorescence, e.g. inherent protein or bacterial UV fluorescence, is taught or suggested by the specification. No other useful identifying characteristic marker other than nucleic acid is taught or suggested by the specification as applicable to a wide range of microorganisms. Other taxonomic markers, such as carotenes/carotenoids, enable identification of only small, well-defined subsets of microorganisms. See generally Nelson et al. (*Applied Spectroscopy Reviews*, 27(1):67-124, **1992**) for discussion of known problems with other types of Raman "fingerprinting"of bacteria, including fluorescence interference, the tendency of bacterial suspensions to aggregate, nonreproducible spectra, etc.

ART BASED REJECTIONS

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chadha et al. (*Review of Scientific Instruments*, 64(11):3088-3093, **1993**) in view of Nelson et al. (*Applied Spectroscopy Reviews*, 27(1):67-124, **1992**) and either Szoka (US 4,483,929) or Newman (US 4,822,566).

Chadha et al. describe a method and an ultraviolet micro-Raman spectrograph therefore for detecting bacterial cells as claimed with the exception of immobilizing the bacterial cells via polylysine instead of the instantly recited antibody. Chadha et al. note on page 3091 (col. 2, ¶2)

> Bacterial cells can be motile and move away from the laser beam. To immobilize bacteria very small volumes of dilute bacterial suspensions were placed on quartz plates coated with 0.01% solution of polylysine and pressed down with a quartz cover slip. Bacterial cells treated in this fashion were fixed on the plates by the polylysine which acted as an adhesive.

Nelson et al. state on page 79, ¶3 that "the DNA and cell surface antigens are in principle the *most attractive targets as potential markers for bacterial identification*" (emphasis added).

Both Szoka (see e.g. ¶ bridging cols. 10-11) and Newman (see e.g. Table 1 in col. 6) describe the conventional use of biospecific antibodies to immobilize bacterial or viral analytes for assay.

It would have been obvious to one of ordinary skill in the art to modify the method and system of Chadha et al. by substituting biospecific antibody for the disclosed polylysine not only because biospecific antibodies are conventionally used to immobilize bacterial and viral analytes for assay, but also because combining the DNA analysis of Chadha et al. with the selectivity/specificity of an antigen-antibody immobilization would combine the two most attractive markers for bacterial identification, as suggested by Nelson et al., thereby resulting in a more efficient identification/detection system and method. No unexpected results are seen. The claimed detection "in the presence of an excess of antibody" is inherent in the UV resonance enhanced Raman method/spectrograph of Chadha et al.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 6 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Malmqvist et al. (US 5,492,840).

Malmqvist et al. describe a surface plasmon resonance biosensor comprising sensing surfaces, each functionalized with analyte-specific antibody; an optical instrumentation unit adapted to direct incident beams of light to each of the sensing surfaces; and, an evaluation unit to convert the detector signal after calibration to the a parameter that is proportional to analyte concentration.

Claim 6 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bogart et al. (US 5,468,606).

Bogart et al. describe a system for detection of an analyte based upon light interference, wherein the device includes a substrate which has an optically active surface exhibiting a first color in response to light impinging thereon and a second color in response to the same light when the analyte is present on the surface. Preferrably, the surface comprises an attachment layer comprising a receptor molecule, e.g. an antibody, which is specifically binds the analyte of interest to the device. Explicitly recited analytes include infectious microorganisms, viruses, Chlamydia, and bacteria.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 6 is rejected under 35 U.S.C. 102(a)/(e) as being clearly anticipated by Herron et al. (US 5,512,492).

Herron et al. describe a system for evanescent light fluoroimmunoassays employing a planar waveguide having capture molecules, e.g. antibodies, immobilized thereon and tracer molecules, e.g. labelled antibodies for detecting analyte.

REMARKS

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Howard et al. (*Applied Spectroscopy*, 34(1):71-75, **1980**) describe a resonance Raman method for the rapid detection and identification of carotene-containing bacteria in water using spectra generated by irradiation at 488.0 and 514.5 nm.

Nelson et al. (US 4,847,198) describe a method and system for identifying bacteria comprising: exciting taxonomic bacterial markers with UV energy such that some of the enery is emitted from the bacteria as a lower resonance enhanced Raman back scattered energy; collecting the resonance enhanced Raman back scattered energy into spectra which corresponds to the taxonomic markers in the bacteria; converting the resonance enhanced Raman back scattered enrgy into spectra which correspond to the taxonomic markers in the bacteria; and, displaying the spectra wherefrom the bacteria are identified.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carol A. Spiegel whose telephone number is (703) 308-3986.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Carol A. Spiegel
October 9, 1997

Carol A. Spiegel
CAROL A. SPIEGEL
PRIMARY EXAMINER
GROUP 1800